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**LAUNDRY DETERGENT: THE TOXICOLOGY  
AND CARCINOGENICITY OF NTA**



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## LAUNDRY DETERGENT: THE TOXICOLOGY AND CARCINOGENICITY OF NTA

### INTRODUCTION

American oncology studies during the mid-1970s indicated a link between a common component of laundry detergent, nitrilotriacetic acid (NTA), and an increased incidence of urinary tract tumours in test mice and rats. This finding raised concern with respect to human exposure to NTA, which has widespread domestic and industrial use, and prompted extensive investigations on the effects of NTA on mammalian and environmental systems. This paper briefly describes the chemical properties of NTA, its role as a detergent component, and the environmental and toxicological assessments conducted so far.

### CHEMISTRY

NTA, first synthesized in 1862, is an aminotricarboxylic acid that can sequester metal ions as water soluble complexes. It is a relatively large molecule with a molecular weight of 191.14 g. Its chemical formula is  $N(CH_2COOH)_3$ . Physically, the central nitrogen atom has a molecule of acetic acid attached at each of its three bonding sites. Chemical manufacturers synthesize NTA in its sodium salt form, in which the hydrogen atom of the acetic acid carboxyl group ( $COOH$ ) is replaced by sodium ( $COONa$ ). The NTA sodium salt has binding properties which make it useful in detergents as a water softener. When NTA is dissolved in water the sodium moiety easily dissociates away from the NTA giving free  $Na^{++}$  ions. This leaves a negatively charged bonding site at the end of each carboxyl group ( $COO^-$ ) which attracts and tightly bonds calcium ( $Ca^{++}$ ) and magnesium ( $Mg^{++}$ ) ions. More simply put, sodium ions





detach from the NTA molecule and are replaced by the causative agents of "hard" water (calcium and magnesium ions), thereby "softening" the water.

## DETERGENTS

A detergent is any material that increases the cleaning effect of water on soiled objects. Laundry detergents are routinely composed of 15-25% surfactants, 30-40% builders, 5% anti-corrosion silicates, and 1% auxiliary agents (optical brighteners, foam stabilizers, enzymes and antiredeposition compounds), with the balance consisting of inert inorganic salts to give the dried product good physical and mechanical properties.

Surfactants, also called surface active agents, greatly lower the surface tension of water. Many substances that can adhere to a fabric exhibit hydrophobicity; that is, they repel water. Reducing surface tension reduces hydrophobicity and allows water to come into contact with the soiled spot. Many surface active agents do not work well in either hard water or water with a low pH value.

Builders, compounds that act as water softeners and deflocculants, contribute greatly to the overall detergent effect. Only three builders are used extensively in detergents: NTA, condensed phosphates (sodium tripolyphosphate, STP), and zeolites. NTA softens the wash water, making the surfactant more active, and it also acts as a deflocculant. Its strong ability to bond with calcium allows it to excise calcium from soil clumps, breaking the calcium bridges that bind soil to itself and to fabrics.

STP used to be the builder compound of choice in detergent formulations. However, the STP released in laundry waste waters was found to degrade to phosphate ( $\text{PO}_4$ ), an essential plant nutrient usually present in natural waters at concentrations low enough to limit vegetative growth. The increased discharge of phosphate into streams and lakes reversed this natural growth limitation and stimulated algae growth; thus severely upsetting the ecological balance in water bodies. Canadian regulations that limited the maximum concentration of elemental phosphorous in laundry detergents to 2.2% (on a weight basis) appeared in the *Canada Gazette, Part II*, on 8 November 1989.



Such stringent regulations to limit the concentration of phosphorous in laundry detergents have forced detergent manufacturers world-wide to use either NTA or zeolites as builders in their products. Natural zeolite is hydrated alkali-aluminum silicate; it has a porous structure and is capable of exchanging alkali ions for calcium and magnesium but it is not highly valued as a building agent. Various forms of synthetically produced zeolite do exhibit excellent deflocculant and water-softening properties. Synthetic zeolite manufacture is a patented process controlled by one chemical company, however; as a result, many detergent manufacturers prefer to use NTA as their builder agent.

## TOXICOLOGY AND ENVIRONMENT STUDIES

### A. Toxicity and Teratology

The minimum lethal oral dose of NTA sodium salt for rats is 4 g per kg body weight.<sup>(1)</sup> Assuming that the toxicity of NTA is constant for all mammals, it would require the ingestion of 227 g (half a pound) of NTA to kill a 57 kg (125 lb.) human being. Thus, NTA is not a very toxic substance.

Chronic dosing of rats and mice with NTA was found to cause dose-dependent health problems and birth defects. This is not unexpected; regular large doses of NTA would continually extract calcium and magnesium, and other positively charged ions from body cells and disrupt their function. In regard to birth defects, induced calcium deficiency in a pregnant mammal would arrest normal foetal bone development. Because a high dose is required to induce such effects in animals, NTA is poorly absorbed by humans, and there is a low environmental concentration of NTA, the International Joint Commission, in its report to The Great Lakes Research Advisory Board (1972), concluded that NTA represents a low health hazard to humans.

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(1) M. Windholz, *et al.* editors, *The Merck Index, An Encyclopedia of Chemicals and Drugs*, 9th edition, Merck & Co., Inc., Rahway, N.J., 1976, p. 854.



## B. Carcinogenicity

The potential of NTA to cause cancer in mice and rats was examined by a number of American laboratories during the mid-1970s.<sup>(2)</sup> In its assessment of the carcinogenicity of NTA, based upon experiments conducted at two different laboratories, the United States National Cancer Institute reported that daily ingestion of diets containing NTA at a concentration of 0.258 g/kg body weight, for periods of up to 24 months, resulted in urinary tract tumours in mice and rats. These studies cannot be regarded as having definitively established NTA as a human carcinogen, however, as the testing procedures did not simulate real-life conditions.

Assuming that humans have the same cancer response to NTA as do rats and mice, daily NTA consumption of 0.258 g/kg body weight per day (14.7 g per day for a 57 kg adult) should induce urinary tract tumours. In Canada, the only non-deliberate source of NTA is drinking water, which, according to the *Canadian Water Quality Guidelines*, has an average concentration of NTA of 2.8 micrograms per litre. Therefore, a 57 kg adult would have to drink 5,252,937 litres of Canadian tap water daily to receive a dose of NTA equivalent to the one that caused cancers in rats and mice.

Such cancer data serve little real-world purpose and raise the question of why they were generated. The international standards for cancer research and carcinogen classification have been established by the International Agency for Research (IARC). Cancer occurrences can be very rare and difficult to correlate with a particular substance in normal environmental or occupational concentrations. In testing, the entire procedure can usually be speeded up by subjecting animals "to a maximum tolerated dose of a substance over their lifetimes."<sup>(3)</sup> In cancer studies, such "heroic dosing" can save both time and money; however, it can also produce data of questionable utility when, as in the case of NTA, massive doses of a mildly toxic substance are administered.

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(2) R.L. Anderson, *et al.*, "A Review of the Environmental and Mammalian Toxicology of Nitritotriacetic Acid," *CRC Critical Reviews in Toxicology*, Vol. 15, p. 1-101, 1985.

(3) R.J. Moolenaar, "Overhauling Carcinogen Classification," *Issues in Science and Technology*, Vol. 8, 1992, p. 70-75.



This aberration in the IARC cancer-testing methodology is a recognized problem and efforts are being made to change either the methodology or the IARC carcinogen classification system.<sup>(4)</sup> Reform is hampered because the world needs a standardized cancer-testing regime and the present system has been in place for some time. Theoretically, the IARC system should not cause problems, for non-real-world data are usually ignored by knowledgeable professionals. The United States Environmental Protection Agency (EPA), however, strictly adheres to the IARC classification system.<sup>(5)</sup> Once the EPA lists a chemical as a possible carcinogen, environmental groups and the media are at liberty to describe that chemical as cancer-causing or as linked to cancer.

On a positive note, the EPA recently announced that it has begun to revise its guidelines for carcinogenic risk assessment with plans to take into consideration "realistic exposure scenarios and mechanisms [of action] when calculating a chemicals's hazard to humans."<sup>(6)</sup>

Following the American NTA carcinogenicity investigation, a large number of independent studies were initiated. All these studies indicated that NTA poses no human health risk at the concentrations to which humans are normally exposed. According to Dr. Robert Squire, Professor, Johns Hopkins University and former Associate Chief of Pathology at the National Cancer Institute, "At the levels that I understand NTA human exposure will occur as a result of detergent use, it [NTA] is completely safe in all respects. In fact the risk of carcinogenic effect at human exposure levels must be considered as virtually zero based on the scientific evidence available."<sup>(7)</sup>

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(4) *Ibid.*

(5) *Ibid.*

(6) D.J. Hanson, "EPA to Revise Cancer Guidelines to Incorporate More Than Tumours," *Chemical and Engineering News*, 26 September 1994, p. 21-22.

(7) Monsanto Canada Inc., "NTA Preparedness Statements Re: Canadian Press Story - March 15/93," Monsanto News Release, p. 6, March 1993.



### C. Environmental Considerations

The environmental effects of NTA have also been well investigated. Although NTA is a large molecule, it is not a complex substance. Its molecular structure, a nitrogen atom and three molecules of acetic acid (vinegar), is easily biodegraded.

A German research scientist, Dr. H. Bernhardt, published a study in 1984 which showed that the NTA concentration in waste water was reduced by over 95% after the water's normal passage through a sewage treatment plant. Lower levels of NTA destruction were observed in sewage treatment plants only (i) at temperatures below 5-7°C, (ii) in instances of high sewage treatment plant loadings (where dilution or sewage washout resulted from heavy storm runoff), or (iii) where bacterial acclimation to NTA had not been established.<sup>(8)</sup> Bacterial populations acclimated to NTA degradation have been isolated in the vicinity of sewage plant outfalls, in groundwater, lakes and rivers. Accordingly, nearly all of the NTA that passes through a sewage treatment plant can be expected to be degraded in the natural environment.

### DISCUSSION

The toxicology, carcinogenicity and environmental fate of NTA have received extensive investigation. This chemical degrades rapidly in the environment and is found as a contaminant of drinking water only at very low concentrations. Human exposure to NTA is so limited as to pose no identifiable health risk. Indeed, NTA is so safe and environmentally benign that Environment Canada has awarded a number of detergents containing NTA its environmental choice "Eco-logo" label.

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(8) H. Bernhardt, *et al.*, *Studie über die aquatische Umweltverträglichkeit von Nitrilotriacetate (NTA)*, Verlag Hans Richarz, Sankt Augustin, 1984.















